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Detailed Action

Claims 34-54 and 63-69 are pending. Claims 34, 41, 42, 47, 49, 50, 54, 55 and 63-67 have been amended by Applicants' amendment filed on 11-09-2009.

The Examiner contacted Applicant's representative, Gary Baker, to discuss rejection of claims under 35 U.S.C. 112, second paragraph, 35 U.S.C. 112, first paragraph.

A draft proposal to cancel claim 51 and to amend claims 34, 36, 41 and 50 was faxed by the Examiner to Applicants to address the remaining rejections of record.

Authorization for the Examiner's amendment was given in a telephone interview with Gary Baker, on December 29, 2010. With respect to the proposed claims, an Examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it must be submitted no later than the payment of the issue fee.

In the claims,

1) Claim 51 have been cancelled.

2) Claims 34, 36, 41 and 50 have been rewritten as follows:

34) A method of incorporating a 5-hydroxy-L- tryptophan (5-HTTP) or a 5-substituted tryptophan unnatural amino acid into a peptide, the method comprising:

preparing a construct comprising a nucleic acid sequence encoding an orthogonal aminoacyl-tRNA synthetase (O-RS) comprising at least 90% identity to SEQ ID NO: 2, the O-RS comprising a proline residue at a position corresponding to position 144 of SEQ ID NO: 2,

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wherein the O-RS aminoacylates a reference orthogonal tRNA (O-tRNA) of SEQ ID No: 3 with a 5-HTTP or a 5-substituted tryptophan analog when the reference O-tRNA, the 5-HTTP or the 5-substituted tryptophan analog, and the O-RS are present in a eukaryotic cell,

preparing a construct comprising a nucleic acid sequence encoding an O-tRNA comprising: at least 90% identity to SEQ ID NO: 3, wherein the O-tRNA is aminoacylated with the 5-HTTP or the 5-substituted tryptophan analog by a reference O-RS of SEQ ID NO: 2 when the reference RS, the 5-HTTP or the 5-substituted tryptophan analog, and the O-tRNA are present in a eukaryotic cell;

introducing the O-RS construct and the O-tRNA construct into the eukaryotic cell; and preferentially, aminoacylating an expressed O-tRNA with the unnatural amino acid, wherein said aminoacylation is catalyzed by an expressed O-RS, wherein the O-tRNA recognizes a selector codon in a nucleic acid sequence encoding the peptide, whereby the 5-HTTP or the 5-substituted tryptophan analog is incorporated into the peptide in the eukaryotic cell.

36) The method of claim 35, further comprising applying a voltage to the peptide, thereby reacting the 5-HTTP with a reactive molecule in the peptide.

41) The method of claim 34, wherein the O-RS construct comprises a nucleic acid comprising a polynucleotide sequence selected from the group consisting of:

- a) a coding polynucleotide sequence of SEQ ID NO: 1,
- b) a coding polynucleotide sequence that encodes the polypeptide of SEQ ID NO: 2,
- c) a complementary sequence of (a) or (b).

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50) The method of claim 34, wherein the O-RS encoding construct and the O-tRNA encoding construct are comprised in the same construct.

Reasons for allowance

The following is an examiner's statement of reasons for allowance: The prior art of record does not teach or suggest:

A method of incorporating a 5-substituted tryptophan unnatural amino acid or a 5-hydroxy-L- tryptophan (5-HHTTP) into a peptide, the method comprising:

preparing a construct comprising a nucleic acid sequence encoding an orthogonal aminoacyl-tRNA synthetase (O-RS) comprising at least 90% identity to SEQ ID NO: 2, the O-RS comprising a proline residue at a position corresponding to position 144 of SEQ ID NO: 2, wherein the O-RS aminoacylates a reference orthogonal tRNA (O-tRNA) of SEQ ID No: 3 with a 5-substituted tryptophan analog or a 5-HHTTP when the reference O-tRNA and the 5-substituted tryptophan analog or 5-HHTTP, and the O-RS are present in a eukaryotic cell,

preparing a construct comprising a nucleic acid sequence encoding an O-tRNA comprising: at least 90% identity to SEQ ID NO: 3, wherein the O-tRNA is aminoacylated with the 5-substituted tryptophan analog or 5-HHTTP by a reference O-RS of SEQ ID NO: 2 when the reference RS, 5-substituted tryptophan analog or 5-HHTTP, and the O-tRNA are present in a eukaryotic cell;

introducing the O-RS construct and the O-tRNA construct into the eukaryotic cell; and, preferentially aminoacylating an expressed O-tRNA with the unnatural amino acid, wherein said aminoacylation is catalyzed by an expressed O-RS, wherein the O-tRNA recognizes a selector codon in a nucleic acid sequence encoding the peptide, whereby the 5-substituted tryptophan unnatural amino acid or the 5-HHTTP is incorporated into the peptide in the eukaryotic cell.

Of note, aminoacyl-tRNA synthetases which covalently link an amino acid to a nucleic acid adaptor molecule, i.e., a tRNA, which contains the triplet anticodon for that amino acid, are well characterized in the art. Additionally, the tRNA structural/functional relationships within segments of the molecule and interactions with translations systems components are well map in

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the art. Also note that a polynucleotide sequence comprising at least 90% identity to a reference tRNA of SEQ ID NO: 3 is free of prior art.

Rejections withdrawn in response to Applicant arguments or amendments:

Claim Rejections - 35 U.S.C. § 112-second paragraph

In view of Applicants' amendment of claim 41 to cancel subparts c)-e), rejection of claims 34-50, 52, 53, 55 and 63-69 under 35 U.S.C. 112, first paragraph, has been withdrawn.

In view of Applicants' amendment of claims 47 and 50, rejection of claims 47 and 50 under 35 U.S.C. 112, second paragraph, has been withdrawn.

Claim Rejections - 35 USC § 112-first paragraph-

In view of Applicants' amendment of claim 41, rejection of claims 34-50, 52, 53, 55 and 63-69 under 35 U.S.C. 112, first paragraph, has been withdrawn.

Claim Objection

In view of Applicants' amendment of claim 41, to cancel subparts c)-e), and furthermore, in view of Applicants arguments insofar as claims 42, objection to claims 41 and 42 under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim, has been withdrawn.

Claim Rejections - 35 USC § 112- First paragraph- New Matter

In view of Applicants' amendment of claim 34 to recite "5- HTTP", rejection of claims 34-55 and 63-69 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description, has been withdrawn.

Conclusion

Claims 34-50, 52-55 and 63-69 are allowable.

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Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria Leavitt whose telephone number is 571-272-1085. The examiner can normally be reached on M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, Ph.D can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1633; Central Fax No. (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Maria Leavitt/

Maria Leavitt
Primary Examiner, Art Unit 1633